

Docket Number: 40225.000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Brookes, et al.
Serial No. : 09/755,747
Examiner : Jeffrey Fredman
Art Unit : 1637
Filed : 5 January 2001
For : DETECTION OF NUCLEIC ACID POLYMORPHISM

DECLARATION OF PUI-YAN KWOK

I, Pui-Yan Kwok, do hereby declare and state as follows.

1. I currently hold the position of Henry Bachrach Distinguished Professor at the University of California in San Francisco. I was assistant and associate professor of medicine at Washington University in St. Louis from 1993 to 2002. I have been an active researcher in the field of nucleic acid analysis and a part of the Human Genome Project since 1990. I have invented 4 DNA detection methods (3 patented) and was the editor of a recent book on the identification and detection of DNA polymorphisms. As a communicating editor of the journal Human Mutation and a member of the editorial board of several scientific journals, I am knowledgeable regarding the field of nucleic acid polymorphism detection. A copy of my curriculum vitae is attached as Exhibit 1.
2. I make this Declaration specifically to address the teachings of Drobyshev et al (Gene 188 (1997) 45 52) and Wittwer et al (US6,174,670). It is my opinion that, as of the priority date of this application, neither Drobyshev et al nor Wittwer et al, either individually or combination with each other or any other teachings then available in the art, would have allowed the ordinarily skilled artisan to perform a DASH method as described

in the specification and pending claims of the above-identified patent application or provided the artisan with a reasonable expectation of successfully discriminating polymorphic alleles by dynamic monitoring of hybridization in solid phase.

3. Prior to the development of the DASH method described in the specification, methods of hybridization involving a nucleic acid molecule bound to a solid surface (i.e. 'solid phase' hybridization) lacked the sensitivity required for the dynamic discrimination of different alleles of a nucleic acid sequence. Dynamic discrimination requires high sensitivity in order that the extent of hybridization can be followed continuously as the temperature is changed. The long exposure times required in previous methods in order to detect surface-bound signal did not allow continuous monitoring and only allowed the static determination of hybridization at a particular temperature.

4. Drobyshev et al describes hybridization of target sequence to oligonucleotides immobilized within a polyacrylamide gel. Oligonucleotides within a gel are disposed in a three-dimensional and random arrangement and an ordinarily skilled artisan would not consider that these gel-immobilized oligonucleotides are 'bound to a solid surface'. This is supported by the finding in Drobyshev et al that the hybridization of the gel-immobilized oligonucleotides resembles liquid phase rather than solid phase hybridization.

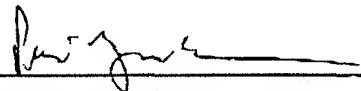
5. Wittwer et al describes a number of PCR based fluorescent methods which *inter alia* distinguish PCR products using SYBR Green I and identify polymorphisms using FRET probes. The methods involve the liquid phase hybridization of amplified DNA strands either with each other or with oligonucleotide probes. None of these methods would lead a worker in the field to the expectation that allelic discrimination could be achieved, in the absence of amplification, using oligonucleotide hybridization on a solid surface using a method as presently claimed.

6. A person working in the field before the priority date would learn nothing from the disclosures of either or both of Wittwer et al and Drobyshev et al which would enable them to perform a DASH method as described in the present claims, nor would the combined teaching of these documents impart any expectation that probe hybridization could be

monitored in real time in the solid phase with sufficient sensitivity to discriminate between alleles of a polymorphism.

7. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: Dec 6, 2002


Pui-Yan Kwok, M.D., Ph.D.

Pui-Yan Kwok, M.D., Ph.D.

CURRICULUM VITAE - Pui-Yan Kwok, M.D., Ph.D.

334-60-1731

December 2002

Personal Information:

Date of Birth: January 6, 1956
Place of Birth: Hong Kong
Citizenship: U.S.A.
Marital Status: Married to Abby A. Li, Ph.D.
Children: Benjamin (7/88), Thomas (11/90), Adam (4/97)

Address and Telephone Numbers:

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Email: kwok@cvmil.ucsf.edu

Present Position: Professor of Dermatology
Henry Bachrach Distinguished Professor and Investigator,
Cardiovascular Research Institute

Education and Experience:

1979 B.A.(Honors), University of Chicago, Chemistry
1981 M.S., University of Chicago, Human Biology
Thesis: Integration of traditional chinese medicine and western
medicine in contemporary China. Mentor: Ralph Nicholas,
Ph.D.
1985 Ph.D., University of Chicago, Organic Chemistry
Dissertation: Total synthesis and enzymatic studies of 10,10-
difluoroarachidonic acid. Mentor: Josef Fried, Ph.D.
1987 M.D., Pritzker School of Medicine, University of Chicago
1987-1988 Intern, Department of Internal Medicine, Rush-Presbyterian-St.
Luke's Medical Center, Chicago, Illinois
1988-1990 Resident, Division of Dermatology, Washington University School
of Medicine, St. Louis, Missouri
1990-1991 Chief Resident, Division of Dermatology, Washington University
School of Medicine, St. Louis, Missouri

Pui-Yan Kwok, M.D., Ph.D.

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|-----------|---|
| 1990-1992 | Postdoctoral Fellow, Division of Dermatology and Department of Genetics, Washington University School of Medicine, St. Louis, Missouri. Mentor: Maynard V. Olson, Ph.D. |
| 1992-1993 | Visiting Scientist, Department of Molecular Biotechnology, University of Washington School of Medicine, Seattle, Washington. Mentor: Maynard V. Olson, Ph.D. |
| 1993-1999 | Assistant Professor of Dermatology and Genetics
Washington University School of Medicine, St. Louis, MO |
| 1999-2002 | Associate Professor of Dermatology and Genetics
Washington University School of Medicine, St. Louis, MO |
| 4/2002 - | Professor of Dermatology
University of California, San Francisco, CA |
| 4/2002 - | Henry Bachrach Distinguished Professor and Investigator
Cardiovascular Research Institute
University of California, San Francisco, CA |

Medical Licensure and Board Certification:

California Medical License (G86455, issued 3/29/2002)
Missouri Medical License (R3J65, 2/1/1989 - 1/31/2004)
Diplomate, American Board of Dermatology, 1991; recertified, 2001

Honors and Awards:

Phi Beta Kappa, University of Chicago, 1979
Medical Alumni Prize for an Outstanding Oral Presentation of Research Performed During Medical School, Pritzker School of Medicine, University of Chicago, 1987
Merck/American Federation for Clinical Research Foundation M.D., Ph.D. Postdoctoral Fellowship Award, 1992
Henry Christian Award for Excellence in Research, Clinical Research Meeting, Washington, DC, May, 1993

Editorial Responsibilities:

Member, Editorial board, Genome Research, 1995 - present
Communicating Editor, Human Mutation, 2001 - present
Member, Editorial Board, Current Pharmacogenomics, 2002 - present
Member, Editorial Board, Human Genomics, 2002 - present
Member, Editorial Board, Human Molecular Genetics, term begins January 2003
Reviewer for Science, Nature, Nature Genetics, Nature Biotechnology, Genome Research, Genomics, Human Genetics, Nucleic Acids Research, and others

Professional Activities:

External Reviewer, Genome Canada, 2001-2002
External Reviewer, Hong Kong Innovation and Technology Fund, 2001-2002
Member, Genome Study Section, CSR, NIH, 1998 - 2001
Ad Hoc member of NIEHS site visits, 1998 - 2001
Member, Scientific Committee, Institute of Biomedical Sciences, Academia Sinica, Taiwan,

Pui-Yan Kwok, M.D., Ph.D.

2002 - present

Professional Societies and Organizations:

American Association for the Advancement of Science
 American Society of Human Genetics
 American Academy of Dermatology
 Society of Investigative Dermatology
 Dermatology Foundation Leaders Society

National and International Meetings and Workshops (last 2 years):

Co-Organizer, Genome Sequencing and Biology Meeting. Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, May 2000 - May 2002
 Member, HGM2002 Scientific Programme Committee. Shanghai, China, April 2002
 Organizer, Workshop on SNP marker genotyping technologies at the American Society of Human Genetics Annual Meeting. Philadelphia, PA, October 2000
 Co-Organizer, Third International Meeting on Single Nucleotide Polymorphism and Complex Genome Analysis. Taos, NM, September 2000
 Member, HGM2003 Scientific Programme Committee. Cancun, Mexico, April 2003

Current Consulting Relationships and Board Memberships:

Member, Scientific Advisory Board, Paternity Testing Corporation, Columbia, MO	1997-present
Consultant, PerkinElmer, Inc. Boston, MA	1998-present
Member, Scientific Advisory Board, Quantum Dot Corporation, Hayward, CA	1998-present
Consultant, Exelixis Pharmaceuticals, Inc., South San Francisco, CA	1999-present
Member, Genome Scientific Advisory Board, Specialty Laboratories, Santa Monica, CA	2000-present
Member, Scientific Advisory Board, Vita Genomics. Taipei, Taiwan	2001-present
Member, Scientific Advisory Board, International Genomics, Ann Arbor, MI	2002-present
Member, Scientific Advisory Board, ParAllele Genomics South San Francisco, CA	2002-present
Member, Scientific Advisory Board, Omicia, Inc. Oakland, CA	2002-present
Member, Scientific Advisory Board, FreshGene, Inc. Concord, CA	2002-present

Pui-Yan Kwok, M.D., Ph.D.

Research Support:

Past Governmental Support (last 3 years):

Principal Investigator, NIH RO1-HG01439 High density genetic map of Xq25-Xq28 1996-1999	Total direct cost:	\$589,000
Principal Investigator, NSF SBR-9610342 Developing genetic markers informative in all populations 1997-1999	Total direct cost:	\$63,000
Principal Investigator, NIH RO1-HG01720 Technologies for diallelic marker discovery and testing 1997-2000	Total direct cost:	\$1,550,000
Program Director, NIH T32-AR07284 Dermatology training grant 1978-2001	Yearly direct cost:	\$181,484
Principal Investigator, NIH RO1-EY12557 New methods for high throughput genome analysis 1998-2002	Total direct cost:	\$374,840
Principal Investigator, NIH RO1-AG16869 Method for global and targeted discovery of SNP markers 1999-2002	Total direct cost:	\$441,000

Past Non-governmental Support (last 3 years):

Principal Investigator, Merck Genome Research Institute #176 New methods for high throughput genome analysis 1998-1999	Total direct cost:	\$65,000
Principal Investigator, The SNP Consortium Allele frequency study 2000-2001	Total direct cost:	\$862,867

Current Governmental Support:

Principal Investigator, NIH RO1-HG01720-04 Characterization of SNP markers 2001-2004	Total direct cost:	\$5,097,295
Project director of Project 1, NIH U01-GM63340-01 "Identification of polymorphisms in members of pathways regulating drug activity" In "Functional polymorphism analysis in drug pathways" (Howard McLeod, P.I.) 2001-2005	Total direct cost (Project 1):	\$733,009

Pui-Yan Kwok, M.D., Ph.D.

Clinical Title and Responsibilities:

Attending physician, Dermatology Outpatient Clinic
Attending physician, Dermatology Consult Service

Past Trainees:

Linda T. Parker, Ph.D., 12/1993-7/1996, patent agent at Hoffman & Baron, LLP,
Parsippany, New Jersey; law student, Rutgers University, New Brunswick, NJ
Xiangning (Sam) Chen, Ph.D., 5/1994-6/1999, Assistant Professor, Virginia
Commonwealth University, Richmond, VA
Zhijie (John) Gu, Ph.D., 11/1996-4/1999, Assistant Professor, Sidney Kimmel
Cancer Center, San Diego, CA
Tony M. Hsu, M.D., 7/1999-6/2001, Resident, Division of Dermatology,
Washington University, St. Louis, MO

Current Trainees:

Ming Xiao, Ph.D., 2/2001-present
Denise Lind, Ph.D., 3/2002 - present

Thesis Committees:

David Politte, Ph.D., 2000 (Washington University)
George Kan, Ph.D., 2002 (Washington University)

Patents:

Kwok, P.-Y. and Chen, X. "Methods and kits for nucleic acid analysis using fluorescence
resonance energy transfer" US05,945,283, issued August 31, 1999.
Kwok, P.-Y. and Chen, X. "Method for nucleic acid analysis using fluorescence
resonance energy transfer" US06,177,249, issued January 23, 2001.
Kwok, P.-Y., Chen, X., and Levine, L. "Fluorescence polarization in nucleic acid
analysis." US06,180,408, issued January 30, 2001.
Kwok, P.-Y., Chen, X., and Levine, L. "Fluorescence polarization in nucleic acid
analysis." US06,440,707, issued August 27, 2002.

Invited Lectures (selected from the last 3 years):

1. Mutation Detection '99 International Workshop, Vicoforte, Italy, May 1999
2. Second International Meeting on Single Nucleotide Polymorphism and Complex Genome
Analysis, Schloss Hohenkammer, Germany, September 1999
3. 2nd Research Symposium on the Genetics of Diabetes, San Jose, CA, October 1999
4. PE Biosystems Sixth Annual Linkage Symposium, San Francisco, CA, October 1999
5. University of Pennsylvania, Philadelphia, PA, January 2000
6. Columbia University, New York, NY, May 2000
7. IBC Annual Pharmacogenomics, SNPs and Genetic Patenting Conference, Princeton, NJ,
May 2000
8. DNA 2000 International Symposium on the State-of-the-Art in Genetic Analysis, Boston,
MA, June 2000
9. National Institute for Aging, Baltimore, MD, July 2000
10. DeCODE Genetics, Reykjavik, Iceland, August 2000
11. Third International Meeting on Single Nucleotide Polymorphism and Complex Genome
Analysis, Taos, New Mexico, September 2000

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12. SNP Genotyping Technologies in the New Millennium Workshop, ASHG Annual Meeting, Philadelphia, PA, October 2000
13. National Institutes of Health, Bethesda, MD, October 2000
14. Johns Hopkins University, Baltimore, MD, December 2000
15. University of Louisville School of Medicine, Louisville, KY, January 2001
16. Duke University, Durham, NC, February 2001
17. Arthritis Foundation "State-of-the-art" Research Research Conference, San Diego, CA, March 2001
18. The Brazilian International Genome Conference, Rio de Janeiro, Brazil, March 2001
19. University of California - San Francisco, San Francisco, CA, April 2001
20. 6th HUGO Mutation Detection Workshop, Bled, Slovenia, May 2001
21. Biogen, Cambridge, MA, May 2001
22. Pharmacia Technology Seminar, St. Louis, MO, June 2001
23. University of California - San Francisco Dermatology Grand Rounds, San Francisco, CA, July 2001
24. SCBA International Symposium, Taipei, Taiwan, August 2001
25. University of Tartu, Tartu, Estonia, September 2001
26. Fifth International Workshop on the Pharmacodynamics of Anti-Cancer Agents, Sea Island, GA, September 2001
27. Hospital for Sick Children, Toronto, ON, Canada, October 2001
28. World Congress of Psychiatric Genetics 2001, St. Louis, MO, October 2001
29. Oregon Health Sciences University, Portland, OR, November 2001
30. Emory University, Atlanta, GA, December 2001
31. University of Chicago, Chicago, IL, March 2001
32. American Association of Cancer Research Annual Meeting, San Francisco, CA, April 2002
33. HGM2002 Satellite Symposium, Hong Kong, April 2002
34. Human Genome Organization HGM2002 Meeting, Shanghai, China, April 2002
35. 6th International Psoriasis Genetics Committee Meeting, Nice, France, April 2002
36. University of Michigan, Ann Arbor, MI, May 2002
37. Endocrine Society Annual Meeting, San Francisco, CA, June 2002
38. 4th Australian Workshop on Mutation Detection, Adelaide, Australia, July 2002
39. Stanford University Genome Technology Center, Stanford, CA, July 2002
40. Molecular Medicine 2002, Reykjavik, Iceland, August 2002
41. Stanford University Symposium on Genetic Studies of Human Disease, Stanford, CA, September, 2002
42. American Society of Human Genetics Annual Meeting, Baltimore, MD, October 2002
43. Institute of Biomedical Sciences, Academia Sinica, Symposium, Taipei, Taiwan, December 2002

Pui-Yan Kwok, M.D., Ph.D.

Bibliography

(Peer-reviewed articles):

1. Kwok P-Y, Stock, LM, and Wright, TL: Partial rate factors for the thallation of toluene. *J. Org. Chem.* 1979;44:2309.
2. Fried, J, Kwok, P-Y, and Muellner, FW: Synthesis and enzymatic studies of fluorinated arachidonic acids. *Advances in Prostaglandin, Thromboxane, and Leukotriene Research* 1987;17B:803-810.
3. Kwok, P-Y, Muellner, FW, Chen, C-K, and Fried, J: Total synthesis of 7,7-, 10,10-, and 13,13-Difluoroarachidonic acids. *J. Am. Chem. Soc.* 1987;109:3684-3692.
4. Kwok, P-Y, Muellner, FW, and Fried, J: Enzymatic conversions of 10,10-Difluoroarachidonic acid with PGH synthase and soybean lipoxygenase. *J. Am. Chem. Soc.* 1987;109:3692-3698.
5. Kwok, P-Y, Gremaud, MF, Nickerson, DA, Hood, L, and Olson, MV: Automatable screening of yeast artificial-chromosome libraries based on the oligonucleotide-ligation assay. *Genomics* 1992;13:935-941.
6. Kwok, P-Y, Carlson, C, Yager, T, Ankener, W, and Nickerson, DA: Comparative analysis of human DNA variations by fluorescence-based sequencing of PCR products. *Genomics* 1994;23:138-144.
7. Gnirke, A, Iadonato, S, Kwok, P-Y, and Olson, MV: Physical calibration of yeast-artificial-chromosome based genome maps by RecA-assisted restriction endonuclease (RARE) cleavage. *Genomics* 1994;24:199-210.
8. Parker, LT, Deng, Q, Zakeri, H, Carlson, C, Nickerson, DA, and Kwok, P-Y: Peak height variations in automated sequencing of PCR products using Taq dye-terminator chemistry. *BioTechniques* 1995;19:116-121.
9. Kwok, P-Y, Deng, Q, Zakeri, H, and Nickerson, DA: Increasing the information content of STS-based genome maps: identifying polymorphisms in mapped STSs. *Genomics* 1996;31:123-126.
10. Parker, LT, Zakeri, H, Deng, Q, Spurgeon, S, Kwok, P-Y, and Nickerson, DA: AmpliTaq DNA polymerase, FS dye-terminator sequencing: analysis of peak height patterns. *BioTechniques* 1996;21:694-699.
11. Chen, X and Kwok, P-Y: Template-directed dye-terminator incorporation (TDI) assay: a homogeneous DNA diagnostic method based on fluorescence energy transfer. *Nucleic Acids Res.* 1997;25:347-353.
12. Chen, X, Zehnbauser, B, Gnirke, A and Kwok, P-Y: Fluorescence energy transfer detection as a homogeneous DNA diagnostic method. *Proc. Natl. Acad. Sci. USA.* 1997;94:10756-10761.
13. Taillon-Miller, P, Bauer-Sardifia, I, Zakeri, H, Hillier, L, Mutch, DG, and Kwok, P-Y: The homozygous complete hydatidiform mole: a unique resource for genome studies. *Genomics* 1997;46:307-310.
14. Pulai, JI, Latour, MA, Kwok, P-Y, and Schonfeld, G: Diabetes mellitus in a new kindred with familial hypobetalipoproteinemia and an apolipoprotein B truncation (apoB-55). *Atherosclerosis* 1998;136:289-295.
15. Chen, X, Livak, K, and Kwok, P-Y: A homogeneous, ligase-mediated DNA diagnostic test. *Genome Res.* 1998;8:549-556.
16. Taillon-Miller, P, Gu, Z, Li, Q, Hillier, L, and Kwok, P-Y: Overlapping genomic sequences: a treasure trove of single nucleotide polymorphisms. *Genome Res.* 1998;8:748-754.
17. Zakeri, H, Amparo, G, Chen, S-M, Spurgeon, S, and Kwok, P-Y: Peak height pattern in dRhodamine and BigDye terminator sequencing. *BioTechniques* 1998; 35:406-414.
18. Pulai, JI, Zakeri, H, Kwok, P-Y, Kim, JH, Wu, J, and Schonfeld, G: Donor splice mutation (665+1 G_T) in familial hypobetalipoproteinemia with no detectable apoB truncation. *Amer. Journ. Med. Gen.* 1998;80:218-220.

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19. Wu, J, Kim, J, Li, Q, Kwok, P-Y, Cole, T, Cefalu, B, Averna, M, Schonfeld, G: Known mutations of apoB account for only a small minority of hypobetalipoproteinemia. *J. Lipid Res.* 1999; 40:955-959.
20. Chen, X, Levine, L, and Kwok, P-Y: Fluorescence polarization in homogeneous nucleic acid analysis. *Genome Res.* 1999;9:492-498.
21. Taillon-Miller, P and Kwok, P-Y: Efficient approach to unique single nucleotide polymorphism discovery. *Genome Res.* 1999;9:499-505.
22. Miller, SE, Taillon-Miller, P, and Kwok, P-Y: Cost-effective staining of DNA with SYBR Green in preparative agarose gel electrophoresis. *BioTechniques* 1999; 27:34-36.
23. Jacobsen, NJ, Lyons, I, Hoogendoorn, B, Burge, S, Kwok, P-Y, O'Donovan, MC, Craddock, N, Owen, MJ: ATP2A2 mutations in Darier's disease and their relationship to neuropsychiatric phenotypes. *Hum. Mol. Genet.* 1999; 8:1631-1636.
24. Marth, GT, Korf, I, Yandell, MD, Yeh, RT, Gu, Z, Zakeri, H, Stitzel, NO, Hillier, L, Kwok, P-Y, Gish, WR: A general approach to single-nucleotide polymorphism discovery. *Nature Genet.* 1999; 23:452-456.
25. Ritter, D, Taylor JF, Hoffmann JW, Carnaghi L, Giddings SJ, Zakeri H, Kwok PY. Alternatively spliced messenger RNA for the alpha-1 subunit of human soluble guanylate cyclase. *Biochem. J.* 2000; 346:811-816.
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27. Taillon-Miller, P and Kwok, P-Y: A High Density Single Nucleotide Polymorphism Map of Xq25-Xq28. *Genomics* 2000; 65:195-202.
28. Taillon-Miller, P, Bauer-Sardina, I, Saccone, NL, Putzel, J, Laitinen, T, Kere, J, Pilia, G, Rice, JP and Kwok, P-Y: Juxtaposed Regions of Extensive and Minimal Linkage Disequilibrium in Human Xq25 and Xq28. *Nature Genet.* 2000; 25:324 -328.
29. Miller, RD, Taillon-Miller, P, and Kwok, P-Y: Evidence from single-nucleotide polymorphisms (SNPs) for natural selection affecting human and orangutan Xq28. *Genomics* 2001; 71:78-88.
30. The International SNP Map Working Group: A map of human genome sequence variation containing 1.4 million SNPs. *Nature.* 2001; 409:928-933.
31. Latif, S, Bauer-Sardina, I, Ranade, K, Livak, K and Kwok, P-Y: Fluorescence polarization in homogeneous nucleic acid analysis II: 5'-nuclease assay. *Genome Res.* 2001; 11:436-440.
32. Marth, G, Yeh, R, Minton, M, Donaldson, R, Li, Q, Duan, S, Davenport, R, Miller, RD, and Kwok, P-Y: Single nucleotide polymorphisms in the public database: how useful are they? *Nature Genetics* 2001; 27:371-372.
33. Collins, A, Ennis, S, Taillon-Miller, P, Kwok, P-Y, Morton, NE: Allelic association with SNPs: Metrics, populations, and the linkage disequilibrium map. *Hum Mutat.* 2001; 17:255-262.
34. Morton, NE, Zhang, W, Taillon-Miller, P, Ennis, S, Kwok, P-Y, Collins, A: The optimal measure of allelic association. *Proc. Natl. Acad. Sci. USA* 2001; 98:5217-5221.
35. Hsu, TM, Law, SM, Duan, S, Neri, BP, Kwok, P-Y: Genotyping single nucleotide polymorphisms by the Invader assay with dual-color fluorescence polarization detection. *Clin. Chem.* 2001; 47:1373-1377.
36. Hsu, TM, Chen, X, Duan, S, Miller, R, and Kwok, P-Y: A universal SNP genotyping assay with fluorescence polarization detection. *BioTechniques* 2001; 31:560-570.
37. Fan, J-B, Surti, U, Taillon-Miller, P, Hsie, L, Kennedy, GC, Hoffner, L, Ryder, T, Mutch, DG, and Kwok, P-Y. Paternal origins of complete hydatidiform moles proven by whole genome SNP haplotyping. *Genomics* 2002; 79:58-62.
38. Vieux, EF, Kwok, P-Y, and Miller, RD. Primer Design for PCR and Sequencing in High Throughput Analysis of SNPs. *BioTechniques* 2002, Suppl:28-30, 32.
39. Speckman, RA, Daw, J, Helms, C, Duan, S, Cao, L, Taillon-Miller, P, Kwok, P-Y, Menter, A, and Bowcock AM. Novel immunoglobulin superfamily gene cluster mapping to a region of human chromosome 17q25 linked to psoriasis susceptibility. *Human Genetics*, in press.

Pui-Yan Kwok, M.D., Ph.D.

40. Ming Xiao, M, Latif, SM, and Kwok, P-Y: Kinetic FP-TDI assay for SNP allele frequency determination. BioTechniques, in press.

Pui-Yan Kwok, M.D., Ph.D.

(Invited articles):

1. Nickerson, DA, Delahunty, C, and Kwok, P-Y: Ligation chain reaction assays and oligonucleotide ligation assays. In: *Current Protocols in Human Genetics* (Dracopoli, NC, et al., Eds.), 1994;2.6.1-10. Wiley-Interscience, New York, NY.
2. Delahunty, C, Kwok, P-Y, and Nickerson, DA: Ligation assays. In: *Molecular Biology and Biotechnology: a Comprehensive Desk Reference* (Meyers, RA, Ed.). VCH Publishers, New York, NY. 1995;491-494.
3. Parker, LT, Zakeri, H, Deng, Q, Spurgeon, S, Kwok, P-Y, and Nickerson, DA: AmpliTaq DNA polymerase, FS dye-terminator sequencing: analysis of peak height patterns. In: *The PCR Technique: DNA Sequencing II* (Gyllenstein, U and Ellingboe, J, Eds.). Eaton Publishing, Natick, MA. 1997;75-84.
4. Kwok, P-Y and Chen, X: Detection of single nucleotide polymorphisms. In: *Genetic Engineering, Principles and Methods* (Setlow, JK, Ed.). Plenum Press, New York, NY. 1998;20:125-134.
5. Landegren, L, Nilsson, M, and Kwok, P-Y: Reading Bits of Genetic Information: Methods for Single-nucleotide Polymorphism Analysis. *Genome Res.* 1998;8:769-776.
6. Gu, Z, Hillier, L, and Kwok, P-Y: Single Nucleotide Polymorphism (SNP) Hunting in Cyberspace. *Human Mutation* 1998;12:221-225.
7. Kwok, P-Y: Genotyping by mass spectrometry takes flight. *Nature Biotechnology* 1998;16:1314-1315.
8. Dietrich, WF, Weber, JL, Nickerson, DA, and Kwok, P-Y: Isolation and analysis of DNA polymorphisms. In: *Mapping Genomes: A laboratory Manual (Genome Analysis, Volume 4)*, (Birren, B, Green, ED, Heiter, P, Klapholz, S, Myers, RM, Riethman, H, and Roskams, J, Eds.). Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY. 1999;135-186.
9. Chen, X and Kwok, P-Y: Homogeneous genotyping assays for single nucleotide polymorphisms with fluorescence energy transfer. *Genetic Analysis (Biomolecular Engineering)* 1998;14:157-163.
10. Kwok, P-Y and Gu, Z: Single nucleotide polymorphism (SNP) libraries: why and how are we building them? *Molecular Medicine Today*, 1999; 5:538-543.
11. Kwok, P-Y: High-throughput genotyping assay approaches. *Pharmacogenomics*, 2000; 1:95-100.
12. Kwok, P-Y and Hsu, T: Keratosis follicularis. In: James, WD, Elston, D. (Chief Eds.); *eMedicine Dermatology*. St. Petersburg: eMedicine Corporation, 2000.
13. Kwok, P-Y: Finding a needle in a haystack: detection and quantification of rare mutant alleles are coming of age. *Clin Chem.* 2000;46:593-594.
14. Kwok, P-Y: Approaches to allele frequency determination. *Pharmacogenomics*, 2000; 1:231-235.
15. Kwok, P-Y: Reflections on a DNA mutation scanning tool. *Nature Biotechnol.* 2001; 19:18-19.
16. Hsu, TM and Kwok, P-Y: Advances in Molecular Medicine. *Journal of the American Academy of Dermatology*, 2001; 44:847-855.
17. White, PS, Kwok, P-Y, Oefner, P, and Brookes, AJ: SNPs: some notable progress. *European Journal of Human Genetics*, 2001; 9:316-318.
18. Brookes AJ, Kwok P-Y, White PS, Oefner PJ: SNiPpers from the Third International Meeting on Single Nucleotide Polymorphism and Complex Genome Analysis, September 8-11, 2000, Taos, New Mexico, USA. *Hum Mutat.* 2001;17:241-242.
19. Kwok, P-Y: Methods for Genotyping Single Nucleotide Polymorphisms. *Annual Review of Genomics and Human Genetics*, 2001; 2:235-258.
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